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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,826	01/25/2001	Yanggu Shi	PF512P1	2604

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EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/768,826	SHI ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' amendment in response to office action dated October 1, 2003 filed on December 12, 2003 is acknowledged. Exhibits A-D attached to the 'Amendment and Response' are acknowledged. Claims 35, 42 and 49 have been amended and entered. Therefore, claims 24-63 are currently pending and are under examination.

Response to Remarks and arguments

Priority Date:

The objection to claiming the filing date of August 15, 2000 of parent application 60/148759 as the priority date is withdrawn in view of Applicants' comments on page 7.

Rejections under 35 USC § 112, First Paragraph

The rejection of claims 30-34, 49, 53, 54 and 60-62 under 35 USC § 112, First Paragraph is withdrawn in view of a declaration regarding availability of the deposit made to ATCC and the ATCC deposit receipt.

Rejections under 35 USC § 112, Second Paragraph

The rejection of claims 29, 32, 41, 46 and 53 under 35 USC § 112, second Paragraph is withdrawn in light of the remarks at page 12-13 of 'Amendment and Response.'

The rejection of claims 30 and 31 under 35 USC § 112, second Paragraph is withdrawn in light of the remarks at page 13-14 of 'Amendment and Response.'

The rejection of claims 35, 42 and 49 under 35 USC § 112, second Paragraph is withdrawn in view of the amendment to the claims.

The rejection of claims 24, 25, 35, 38, 42, 45, 49, 52, 56, 57, 60, 61 under 35 USC § 112, second Paragraph is withdrawn in view of the remarks on page 12.

Rejections under 35 USC § 102

The rejection of claims 24-26, 30 and 31 under 35 USC § 102 is withdrawn in view of the response and remarks on page14-15 of 'Amendment and Response.'

Claim Rejections – 35 USC § 101

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

Claims 24-63 remain/are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The claimed polypeptides are not supported by either a specific asserted utility or a well established utility because the specification fails to assert any utility for the claimed polypeptides or the encoded proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed polypeptides such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be assessed. The reasons are as follows:

The specification, on page 69 (Gene18) and page 73 (Table 1) describes clone HBIMF63 (ATCC NO: PTA-536) to which the instant invention relates. The specification asserts (page 69) that translation product of this gene shares sequence homology with ligand binding protein which is thought to be important in cell-to-cell communication and signal transduction. Further, the translation product of this gene also shares sequence homology with lymphocytoma proliferation activating peptide (LPAP). Based on the specification (pages 69-72); and Examples 5-8, no biological activity has been set forth for the polypeptide of clone HBIMF63 nor any use for the polypeptide itself has been provided. Only speculative biological activities have been provided on page 130-147, 167-275 of the specification. In examples 1-58, it appears that these experiments have not been performed because the examples are not written in the past tense. Therefore, they appear to be prophetic examples ((MPEP 608.01 (p)). For example, the use of

the protein for further research is described here (page 167-170). This use is not a patentable utility because one skilled in the art should not have to discover for themselves the use of the claimed proteins. This situation requires carrying out future research to identify or reasonably confirm a "real world" context of use and therefore does not define specific and substantial utility.

Other activities that the protein may exhibit are listed throughout page 275-277 of the specification. However, these activities are speculative. In summary, the proteins claimed do not have a credible, specific or well-established or even demonstrable utility and therefore lacks utility under 35 U.S.C. 101.

Claims 24, 25, 26, 35, 38, 42, 45, 49, 52, 56, 57, 60 and 61, are drawn to a protein comprising a sequence of SEQ ID 47 and fragments thereof. The specification does not describe the functional properties of the entire protein or its fragments, and the structural information is limited. While the specification enumerates several known assays for biological activity (p. 316-329, Examples 13-20), it does not guide the selection of a specific assay that would be used to screen the biological activities of the claimed fragments for which no known activity is explicitly disclosed nor demonstrated.

Claims 30, 31, 33, 49, 54, 60, 61, and 62 are drawn to proteins or a fragment encoded by the cDNA of clone HBIMF63. It is not clear from the description of the clone (specification page 69-72, 96-100) about the protein structure, aside from its amino acid sequence, and/or its function. As discussed above, based on the specification (page 69-72, 96-100) it is unclear what activity the claimed proteins or protein fragments possess or how a person having skill in the art would have used the claimed proteins.

Claims 27, 33, 39, 47, 54, 58, and 62 are drawn to a protein of claims 24, 32, 35, 46, 53, 56 and 60 respectively, which comprises a heterologous polypeptide sequence. It is not clear from the description on page 145-147 and page 306 (Example 9) what is the heterologous protein's structure, and /or its function.

Claims 28, 34, 40, 48, 55, 59 and 63 are directed to a composition comprising the protein of claims 24, 32, 35, 46, 53, 56, 60 respectively and a pharmaceutically acceptable carrier. The

speculative composition and their administration and dosage are listed in the specification (pages 331-356, Example 23), however, when the proteins claimed lack a credible, specific or well established utility, the composition of those proteins would also lack utility under 35 U.S.C. 101. Applicants assert on page 331 that the composition would be useful in the treatment of conditions associated with disease. Examples of many therapeutic methods have been described in pages 331-356 but the specification does not indicate explicitly the correlation of the role of the protein or the composition containing the protein to a specific disease treatment.

Claims 29, 32, 41, 46 and 53 are drawn to a protein produced by the method comprising expressing the protein by a cell and recovering the protein. Specification on page 147-159 describes the vectors and host cells but does not indicate the function of the expressed protein.

Claims 35, 42 and 49 and dependent claims 36, 37, 43, 44, 50, 51 thereto are drawn to an isolated first polypeptide at least 90% identical to a second polypeptide comprising amino acid sequence of SEQ ID NO: 47 and fragments thereof, wherein said first polypeptide is used to generate or select an antibody that specifically binds said second polypeptide. The specification at page 99, lines 2-10 while defining "functional activity" of a polypeptide, indicates that such functional activities include biological activity, antigenicity, immunogenicity etc. etc. However, specification fails to describe or demonstrate any such activity of the claimed protein that can be correlated with the antigenicity or immunogenicity activity, moreover, no such activity of the claimed protein has been demonstrated using Western Blot and ELISA as claimed in claims 36, 37, 43, 44, 50, 51.

In the instant case, the failure of the specification to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the protein set forth in SEQ ID NO: 47 other than the fact that the protein shares homology with ligand binding protein (p. 69). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 47 based on its structure alone for the reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general

assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

The rejection has been set forth in the previous office action. In response, applicants traverse the foregoing rejection and argue (pages 4-10), that the burden is on the Examiner to provide support that asserted utility is neither specific nor substantial. Applicants submit in the remarks (see page 8, paragraph 2) that they have only provided an asserted utility, further Applicants state that the Examiner has acknowledged that Applicants have asserted utilities in the specification, the utilities are dismissed as being insubstantial or non-specific. The arguments are not persuasive because it should be noted that the claimed subject matter is not supported by a specific utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. In response it has been stated that (see page 8, paragraph 3) Applicants assert in the specification that the claimed gene (Gene 18) is expressed in ovarian cancer (Grade II papillary carcinoma). In addition they state that 'expression of this gene at significantly higher or lower levels **may be** routinely detected in certain tissues or cell types... or bodily fluids ... or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level."(page 70, lines 25-29). Therefore, Applicants submit that this assay combined with the female reproductive disorder discloses in the specification supports that their asserted utility is substantial. The arguments are considered fully but not found persuasive because no evidence is provided to support this assertion that each polynucleotides and polypeptides of the invention is specifically expressed in the said tissues and not in other tissues. Therefore, identifying and studying the properties of the claimed subject matter itself or the mechanisms in which the claimed subject matter is involved does not define a "real world" context of use. Thus the asserted utility is not substantial.

Applicants further assert that SEQ ID NO: 47 is the **likely** human homolog of rat ligand binding protein, known in the art as RYD5, which shares sequence homology to both rat and human Clara cell secretory protein (CC10; also known as uteroglobin or CC16). CC10 is

expressed predominantly by mucosal epithelial cells in the lung, uterus and prostate and is a regulator involved in inflammation and malignant transformation in the respiratory and urogenital fields (Shijubo et al, Exhibit A), furthermore, the highest levels of CC10 expression in the endometrium occur during mid-luteal phase (Muller-Schottle et al, Exhibit B). Applicants noted that the mid-luteal phase corresponds to extensive vascularization during the menstruation cycle. Applicants point out that it was well known in the art that at the time the invention is filed that a strong correlation exists between vascularization and tumor formation (Herblin et al, Exhibit C). Applicants' attempt to establish a correlation between the protein set forth in SEQ ID NO: 47 of instant application and a ligand binding protein RYD5 by citing Exhibits A, B and C have been considered. However, it should be noted that the specification fails to provide a sequence homology of the protein of SEQ ID NO: 47 to the sequence of a ligand binding protein, also there is no description in the specification or in the Exhibit A about a homology between RYD5 and CC10. Regarding the highest levels of CC10 or CC16 (uteroglobin) expression in the endometrium occurring during mid-luteal phase (Exhibit B), has no correlation between the claimed protein and uteroglobin protein of Exhibit C. Applicants' observation and the statement regarding a strong correlation between vascularization and tumor formation (Herblin et al, Exhibit C) have been noted. The Exhibit C has reported that the inhibition of angiogenesis results in the suppression of tumor growth, however, this report does not support the findings in present invention because the specification does not provide any activity of the claimed protein that could be correlated with the activity of an angiogenic protein of Exhibit C. Further, Applicants have stated, that according to Utility Guidelines ....'the assertion on homology to existing nucleic acids or protein having an accepted utility, the asserted utility must be accepted by the Examiner. In response it should be noted that as discussed above the specification and Exhibits fail to describe or demonstrate any homology of the claimed protein to RYD5 and/or CC10 or CC16, which has accepted utility. Also the extrapolation from the sequence homology cannot establish the biological function or activity of the protein. Therefore, the response fails to establish a probative relation between the evidence of record (Exhibits A-C) and the properties of the claimed protein.

Regarding citation of Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) Applicants comment on page 9, that the instant case is not analogous to the situation in Brenner v. Manson. In Brenner, the Applicant was trying to establish an earlier date of invention for the purpose of provoking an interference. In response Applicants should note that the Examiner's reliance upon Brenner was only for the conclusion reached by the courts regarding the use of a product in further research, "Congress intended that no patent be granted on a chemical compound whose sole 'utility'consists of its potential role as an object of use-testing." Brenner, 148 USPQ 689. Thus, instant polypeptide is in a similar category to the Brenner, because the claimed polypeptide needs to be used for further research (see discussion supra).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-63 remain/are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial or well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (571) 272-0951. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547

Rita Mitra, Ph.D.
March 19, 2004

ROBERT A. WAX
PRIMARY EXAMINER